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LETTERS TO THE EDITOR

RE: "RELATION OF CIGARETTE SMOKING TO NON-HODGKIN'S LYMPHOMA AMONG MIDDLE-AGED MEN"

The recent paper by Freedman et al. (1) presented results which suggested that heavy cigarette smoking may be an important risk factor for non-Hodgkin's lymphoma among young and middle-aged men but not among older individuals. They found a relation between cigarette smoking and non-Hodgkin's lymphoma among men aged 32–60 years, particularly among heavy smokers (≥50 pack-years), men who smoked ≥2.5 packs of cigarettes per day, and men who had smoked for 30–39 years, but not in the older age group, which has predominated in most previous studies of non-Hodgkin's lymphoma. The study results also suggested that age at initiation of smoking and number of years since smoking cessation were related to non-Hodgkin's lymphoma. The findings by Freedman et al. (1) prompted us to reanalyze our data on non-Hodgkin's lymphoma and smoking (2) according to the same parameters.

Our previous report, on a pooled analysis of three population-based case-control studies carried out in Nebraska, Kansas, and Iowa/Minnesota (2), showed no relation between cigarette smoking and non-Hodgkin's lymphoma among men, but the age range of our cases and controls was 21–100 years, much wider than the range of 32–60 years

TABLE 1. Relation of cigarette smoking to non-Hodgkin's lymphoma among men in three US case-control studies, by age at diagnosis

	Age group											
	21–31 years				32–60 years				≥61 years			
	No. of controls	No. of cases	OR*,†	95% CI*	No. of controls	No. of cases	OR†	95% CI	No. of controls	No. of cases	OR†	95% CI
Smoking status‡												
Never smoker	81	6	1.0§		232	93	1.0§		629	235	1.0§	
Ever smoker	55	9	3.0	0.8, 11.6	627	249	1.0	0.7, 1.3	1,275	400	0.8	0.7, 1.0
Current smoker	34	6	2.7	0.6, 12.3	326	132	1.0	0.7, 1.4	399	135	0.8	0.6, 1.1
Former smoker¶	21	3	3.6	0.6, 21.1	280	112	1.0	0.7, 1.4	805	240	0.8	0.6, 0.9
Age (years) started smoking#												
≥24	1	0			38	20	1.5	0.8, 2.9	179	43	0.6	0.4, 0.9
21–23	2	0			55	20	0.9	0.5, 1.5	112	45	1.0	0.7, 1.4
18–20	17	3	3.2	0.5, 19.7	229	88	1.0	0.7, 1.4	386	124	0.8	0.6, 1.0
15–17	22	5	3.9	0.8, 19.1	205	86	1.0	0.7, 1.4	327	108	0.8	0.6, 1.1
<15	13	1	1.8	0.2, 18.7	83	31	0.9	0.6, 1.5	147	49	0.8	0.6, 1.2
No. of packs smoked per day#												
<0.5	8	0			41	17	0.9	0.5, 1.7	145	69	1.2	0.9, 1.7
0.5–0.9	14	3	3.8	0.6, 23.5	89	37	1.1	0.7, 1.7	215	75	0.9	0.7, 1.2
1.0–1.4	20	4	2.7	0.5, 15.4	238	104	1.1	0.8, 1.6	474	134	0.7	0.5, 0.9
1.5–1.9	7	1	3.2	0.3, 37.3	84	36	1.0	0.6, 1.6	117	36	0.8	0.5, 1.2
2.0–2.4	4	0			116	34	0.7	0.4, 1.1	164	41	0.6	0.4, 0.9
≥2.5	2	0			48	18	1.0	0.5, 1.9	68	24	0.9	0.5, 1.5
Years of smoking#												
<10	25	4	3.1	0.6, 14.9	72	23	0.8	0.4, 1.3	60	35	1.4	0.9, 2.2
10–19	30	5	2.9	0.6, 14.9	128	54	1.2	0.8, 1.8	91	30	0.8	0.5, 1.3
20–29	0	0			173	71	1.0	0.7, 1.5	124	42	0.8	0.5, 1.2
30–39	0	0			160	63	0.9	0.6, 1.4	212	54	0.6	0.4, 0.9
≥40	0	0			76	34	1.0	0.6, 1.7	664	206	0.8	0.6, 1.0
Pack-years of smoking#												
<20	50	8	2.5	0.6, 10.0	202	75	1.0	0.7, 1.4	262	103	1.0	0.7, 1.3
20–49	5	0			254	119	1.1	0.8, 1.6	426	119	0.7	0.5, 0.9
≥50	0	0			145	48	0.8	0.5, 1.2	419	133	0.8	0.6, 1.1
Years since quitting smoking#												
1–4	11	1	2.8	0.3, 29.5	64	28	1.2	0.7, 2.1	131	37	0.8	0.6, 1.1
5–9	10	2	4.5	0.5, 40.4	50	15	0.8	0.4, 1.5	119	27	0.7	0.5, 1.1
10–15	0	0			64	27	1.0	0.5, 1.6	144	33	0.6	0.4, 0.9
≥16	0	0			102	42	1.0	0.6, 1.5	411	143	0.9	0.7, 1.1

* OR, odds ratio; CI, confidence interval.
† Adjusted for age, state of residence, and respondent type, compared with nonsmokers.
‡ Some smokers could not be classified as current or former smokers because of missing values for either age at starting to smoke or years of smoking.
§ Reference group.
¶ Men were considered former smokers if they reported having stopped smoking ≥1 year before diagnosis (cases), interview (living controls), or death (proxy controls).
# Men who were missing information in this category were excluded only from the analyses for which data were missing.

studied by Freedman et al. (1). In table 1, we present our data in three age groups: 21–31, 32–60, and ≥61 years. Odds ratios and 95 percent confidence intervals were calculated using conditional logistical regression, adjusting for state of residence, age, and interview status (proxy or direct).

Compared with men who had never smoked cigarettes, the risks among ever smokers, current smokers, and former smokers were not significantly increased in any age group. There were no trends in risk by age at initiation of smoking, number of packs smoked per day, years smoked, pack-years, or years since quitting smoking. In fact, in the 32–60 age group, the odds ratio was greater among men who had started smoking cigarettes after age 23 (odds ratio (OR) = 1.5) than among men who had started smoking earlier (OR = 0.9 or 1.0, depending on the age). The odds ratio was greater among men who had stopped smoking 1–4 years previously (OR = 1.2) than among men who had stopped 5–9 (OR = 0.8), 10–15 (OR = 1.0), or ≥16 years previously (OR = 1.0), but none of these odds ratios were statistically significant. Among men over the age of 60, slightly decreased risks of non-Hodgkin's lymphoma were observed with various measures of smoking. In the 21–31 years age group, risk increased with several measures of smoking, but no consistent trends were observed. We hesitate to draw any conclusions about smoking and risk of non-Hodgkin's lymphoma in 21- to 31-year-old men, because our sample size was very small and none of the odds ratios were statistically significant.

Our results showed no support for a relation between smoking and an increased risk of non-Hodgkin's lymphoma among men in any age group. We did not see dose-response relationships by number of cigarettes smoked, years smoked, pack-years of smoking, or early age at smoking initiation for any age group. There were some differences in risk between our three age groups. We found nonsignificant suggestions of increased risk among younger men and of decreased risk among older men, but no elevation in relative risk for the 32–60 age group as Freedman et al. (1) observed.

References

1. Freedman DS, Tolbert PE, Coates R, et al. Relation of cigarette smoking to non-Hodgkin's lymphoma among middle-aged men. Am J Epidemiol 1998;148:833–41.
2. Zahm SH, Weisenburger DD, Holmes FF, et al. Tobacco and non-Hodgkin's lymphoma: combined analysis of three case-control studies (United States). Cancer Causes Control 1997;8:159–66.

Barry L. Waddell
Howard Hughes Medical Institute
National Institutes of Health
Research Scholar
Aaron Blair
Shelia Hoar Zahm
Division of Cancer Epidemiology and
Genetics
National Cancer Institute
Bethesda, MD 20892

THE FIRST AUTHOR REPLIES

We thank Waddell et al. (1) for their comments on our recent article (2). It should be emphasized that we found the association between cigarette smoking and non-Hodgkin's lymphoma (NHL) to be strongest among men who had smoked ≥50 pack-years (odds ratio = 1.6) and among younger men (<50 years of age). There was only a small increase in risk (odds ratio = 1.17) among current smokers in the entire sample. The results of Waddell et al. (1) indicating that the risk for NHL is not increased among 32- to 60-year-old cigarette smokers are interesting, but several points should be considered when comparing the results of these two analyses.

Based on an examination of sample sizes in a previous report on the three cited case-control studies (3), it appears that proxy respondents provided information on cigarette smoking for a substantial proportion (~one third) of the controls in Waddell et al.'s table 1. This previous report (3) found the duration and intensity of cigarette smoking to be inversely related to NHL among proxy respondents, possibly because of an increased risk of death from various causes among smokers (4). Since Zahm et al. concluded then that "for smoking, it would be better to base this study's conclusion on the living subjects only" (3, p. 164), it is interesting that the new table includes deceased controls; this may have biased several of the findings towards the null hypothesis. Deceased controls were not included in our analyses (2), and it would be interesting to see the results of table 1 after exclusion of the deceased controls.

Comparable to our results concerning an interaction with age, the findings in table 1 (although based on very small numbers) also suggest that young smokers may be at increased risk for NHL. It would be interesting to examine the results of a stratified analysis of men in the 32- to 60-year age group. Is there an association between smoking and NHL among men under 50 years of age? It should also be noted that the number of NHL cases (n = 1,193) in our study (2) is about 3.5 times as large as the number of 32- to 60-year-old cases (93 + 249 = 342) shown in table 1.

We thank Waddell et al. (1) for sharing their results, and we feel that additional study of the relation of cigarette smoking to NHL among middle-aged men is warranted. Particular attention should be given to the use of proxy information on cigarette smoking and possible effect modification by age.

References

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2. Freedman DS, Tolbert PE, Coates R, et al. Relation of cigarette smoking to non-Hodgkin's lymphoma among middle-aged men. Am J Epidemiol 1998;148:833–41.
3. Zahm SH, Weisenburger DD, Holmes FF, et al. Tobacco and non-Hodgkin's lymphoma: combined analysis of three case-control studies (United States). Cancer Causes Control 1997;8:159–66.
4. McLaughlin JK, Blot WJ, Mehl ES, et al. Problems in the use of dead controls in case-control studies. I. General results. Am J Epidemiol 1985;121:131–9.

David S. Freedman
National Center for Chronic Disease
Prevention and Health Promotion
Centers for Disease Control and
Prevention
Atlanta, GA 30341